

| Table S1 SNPs used as instrument variables from gut microbiota and PTB | | | | | | | | | | |
|--|-------------|---------------|--------------|----------------|-------|-------------|---------|-------|---------|--------------|
| Bacterial taxa | SNP | Effect allele | Other allele | Gut microbiota | | | Outcome | | | F Statistics |
| | | | | Beta | SE | P value | Beta | SE | P value | |
| <i>Coprococcus2</i> | rs10070053 | A | G | 0.059 | 0.014 | 7.64883E-06 | -0.033 | 0.020 | 0.020 | 19.27267485 |
| <i>Coprococcus2</i> | rs12634070 | T | C | 0.074 | 0.016 | 9.95104E-06 | 0.015 | 0.023 | 0.023 | 19.94192282 |
| <i>Coprococcus2</i> | rs2482516 | C | T | 0.075 | 0.016 | 4.72333E-06 | -0.050 | 0.024 | 0.024 | 21.00165357 |
| <i>Coprococcus2</i> | rs35890118 | A | G | -0.067 | 0.015 | 8.25962E-06 | 0.010 | 0.023 | 0.023 | 20.30358999 |
| <i>Coprococcus2</i> | rs61823518 | A | C | -0.096 | 0.022 | 6.68258E-06 | -0.009 | 0.033 | 0.033 | 19.61310923 |
| <i>Coprococcus2</i> | rs6677933 | C | T | -0.080 | 0.016 | 1.18502E-06 | 0.025 | 0.028 | 0.028 | 23.99433146 |
| <i>Coprococcus2</i> | rs72680320 | T | C | -0.065 | 0.014 | 2.27115E-06 | 0.020 | 0.021 | 0.021 | 21.76587244 |
| <i>Coprococcus2</i> | rs9426473 | A | G | 0.073 | 0.016 | 6.30687E-06 | -0.014 | 0.023 | 0.023 | 20.24313698 |
| <i>Escherichia Shigella</i> | rs112767262 | T | C | 0.073 | 0.016 | 8.20636E-06 | 0.009 | 0.024 | 0.709 | 20.07474534 |
| <i>Escherichia Shigella</i> | rs113127095 | A | G | 0.151 | 0.032 | 3.33349E-06 | 0.039 | 0.050 | 0.438 | 21.79852687 |
| <i>Escherichia Shigella</i> | rs113513883 | A | G | 0.172 | 0.038 | 5.27716E-06 | 0.039 | 0.057 | 0.496 | 20.51038272 |
| <i>Escherichia Shigella</i> | rs1154904 | A | G | -0.061 | 0.013 | 3.03751E-06 | 0.009 | 0.020 | 0.635 | 22.04270298 |
| <i>Escherichia Shigella</i> | rs118526 | C | A | -0.059 | 0.014 | 7.99566E-06 | -0.030 | 0.022 | 0.174 | 19.10733655 |
| <i>Escherichia Shigella</i> | rs2798105 | A | G | -0.101 | 0.022 | 8.24501E-06 | 0.000 | 0.034 | 0.990 | 20.6285257 |
| <i>Escherichia Shigella</i> | rs4731451 | G | A | -0.061 | 0.014 | 7.4731E-06 | -0.019 | 0.021 | 0.375 | 20.36153632 |
| <i>Escherichia Shigella</i> | rs57024273 | T | C | 0.063 | 0.014 | 9.70465E-06 | -0.004 | 0.023 | 0.849 | 20.02755698 |
| <i>Escherichia Shigella</i> | rs592299 | T | C | -0.059 | 0.013 | 4.76927E-06 | -0.048 | 0.020 | 0.016 | 20.90225134 |
| <i>Escherichia Shigella</i> | rs73208162 | A | G | -0.119 | 0.025 | 2.19391E-06 | -0.045 | 0.058 | 0.439 | 23.0660382 |
| <i>LachnospiraceaeNK4A136group</i> | rs10952110 | G | T | 0.049 | 0.011 | 9.08113E-06 | 0.018 | 0.020 | 0.365 | 19.79599978 |
| <i>LachnospiraceaeNK4A136group</i> | rs11263806 | A | G | -0.052 | 0.012 | 5.06517E-06 | 0.008 | 0.021 | 0.722 | 20.18832404 |
| <i>LachnospiraceaeNK4A136group</i> | rs12611395 | A | G | -0.090 | 0.020 | 5.83039E-06 | -0.022 | 0.033 | 0.500 | 20.43467827 |
| <i>LachnospiraceaeNK4A136group</i> | rs160061 | A | G | 0.051 | 0.011 | 2.12198E-06 | 0.009 | 0.020 | 0.671 | 22.5958203 |
| <i>LachnospiraceaeNK4A136group</i> | rs28540839 | A | C | 0.051 | 0.011 | 9.34319E-06 | 0.001 | 0.020 | 0.965 | 21.12353032 |
| <i>LachnospiraceaeNK4A136group</i> | rs2880566 | T | C | 0.060 | 0.013 | 5.61428E-06 | 0.004 | 0.028 | 0.890 | 19.81507439 |
| <i>LachnospiraceaeNK4A136group</i> | rs4955932 | T | C | -0.049 | 0.011 | 7.05426E-06 | -0.031 | 0.021 | 0.130 | 20.2527293 |
| <i>LachnospiraceaeNK4A136group</i> | rs59805249 | T | C | 0.094 | 0.021 | 9.45385E-06 | 0.003 | 0.034 | 0.920 | 20.26007118 |
| <i>LachnospiraceaeNK4A136group</i> | rs68104925 | T | C | -0.055 | 0.012 | 2.36779E-06 | -0.002 | 0.022 | 0.919 | 22.6465146 |
| <i>LachnospiraceaeNK4A136group</i> | rs7073658 | T | G | -0.050 | 0.011 | 5.2691E-06 | -0.005 | 0.020 | 0.786 | 20.74520113 |
| <i>LachnospiraceaeNK4A136group</i> | rs73044693 | A | G | -0.108 | 0.023 | 3.57256E-06 | 0.000 | 0.040 | 0.993 | 21.89954386 |
| <i>LachnospiraceaeNK4A136group</i> | rs7616165 | G | T | -0.231 | 0.048 | 2.77391E-06 | 0.052 | 0.066 | 0.432 | 22.73852735 |
| <i>LachnospiraceaeNK4A136group</i> | rs76193507 | A | G | -0.230 | 0.050 | 2.9309E-06 | -0.070 | 0.035 | 0.048 | 21.12893409 |
| <i>LachnospiraceaeNK4A136group</i> | rs7832116 | A | G | -0.071 | 0.015 | 3.57084E-06 | -0.029 | 0.030 | 0.330 | 22.19822471 |
| <i>LachnospiraceaeNK4A136group</i> | rs954878 | A | G | -0.052 | 0.011 | 1.78203E-06 | -0.009 | 0.021 | 0.668 | 22.78169161 |

Table S2 The heterogeneity results from MR-PRESSO

| Bacterial taxa | P value |
|------------------------------------|----------------|
| <i>Coprococcus2</i> | 0.579 |
| <i>Escherichia_Shigella</i> | 0.711 |
| <i>LachnospiraceaeNK4A136group</i> | 0.964 |

Table S3 Directional pleiotropy results from Egger intercept analysis

| Bacterial taxa | Egger intercept | SE | P value |
|------------------------------------|-----------------|-------|---------|
| <i>Coproccus2</i> | -0.07 | 0.066 | 0.331 |
| <i>Escherichia_Shigella</i> | 0.008 | 0.026 | 0.756 |
| <i>LachnospiraceaeNK4A136group</i> | 3.80413E-05 | 0.013 | 0.998 |

Table S4 The heterogeneity results from the Cochran's Q test

| Bacterial taxa | MR-Egger | | IVW | |
|------------------------------------|----------|---------|-----|---------|
| | Q | P value | Q | P value |
| <i>Coprococcus2</i> | 6 | 0.585 | 7 | 0.563 |
| <i>Escherichia_Shigella</i> | 8 | 0.621 | 9 | 0.706 |
| <i>LachnospiraceaeNK4A136group</i> | 13 | 0.955 | 14 | 0.972 |

Table S5 Leave-one-out analysis for IVW-RE MR of gut microbiota on PTB

| Bacterial taxa | SNP | Beta | SE | P value |
|-------------------------------------|-------------|------------|------------|------------|
| <i>Coprococcus</i> 2 | rs10070053 | -0.1883612 | 0.1240587 | 0.12893287 |
| <i>Coprococcus</i> 2 | rs12634070 | -0.3034096 | 0.1257859 | 0.01586045 |
| <i>Coprococcus</i> 2 | rs2482516 | -0.1654243 | 0.12541 | 0.18714631 |
| <i>Coprococcus</i> 2 | rs35890118 | -0.2432664 | 0.1239355 | 0.04966403 |
| <i>Coprococcus</i> 2 | rs61823518 | -0.2751835 | 0.1241259 | 0.02662504 |
| <i>Coprococcus</i> 2 | rs6677933 | -0.2219418 | 0.1235383 | 0.07240821 |
| <i>Coprococcus</i> 2 | rs72680320 | -0.2206758 | 0.1247554 | 0.07691599 |
| <i>Coprococcus</i> 2 | rs9426473 | -0.2376327 | 0.1257102 | 0.05871495 |
| <i>Escherichia Shigella</i> | rs112767262 | 0.2381885 | 0.1175336 | 0.04270775 |
| <i>Escherichia Shigella</i> | rs113127095 | 0.2206573 | 0.1172507 | 0.05984596 |
| <i>Escherichia Shigella</i> | rs113513883 | 0.2246727 | 0.117327 | 0.05550168 |
| <i>Escherichia Shigella</i> | rs1154904 | 0.2746045 | 0.1176747 | 0.01961721 |
| <i>Escherichia Shigella</i> | rs118526 | 0.1976337 | 0.1159738 | 0.08835793 |
| <i>Escherichia Shigella</i> | rs2798105 | 0.2534056 | 0.1173198 | 0.03077609 |
| <i>Escherichia Shigella</i> | rs4731451 | 0.2152958 | 0.1165675 | 0.06475252 |
| <i>Escherichia Shigella</i> | rs57024273 | 0.2543007 | 0.1160091 | 0.02837407 |
| <i>Escherichia Shigella</i> | rs592299 | 0.1546702 | 0.1170076 | 0.18620765 |
| <i>Escherichia Shigella</i> | rs73208162 | 0.216558 | 0.1135813 | 0.056568 |
| <i>Lachnospiraceae</i> NK4A136group | rs10952110 | 0.1592312 | 0.08745613 | 0.06865273 |
| <i>Lachnospiraceae</i> NK4A136group | rs11263806 | 0.1832145 | 0.08757427 | 0.03642918 |
| <i>Lachnospiraceae</i> NK4A136group | rs12611395 | 0.1639728 | 0.0880765 | 0.06264418 |
| <i>Lachnospiraceae</i> NK4A136group | rs160061 | 0.1686041 | 0.08771522 | 0.05458356 |
| <i>Lachnospiraceae</i> NK4A136group | rs28540839 | 0.1759334 | 0.08766744 | 0.04476813 |
| <i>Lachnospiraceae</i> NK4A136group | rs2880566 | 0.171939 | 0.08700077 | 0.04812167 |
| <i>Lachnospiraceae</i> NK4A136group | rs4955932 | 0.1482599 | 0.08739813 | 0.08981505 |
| <i>Lachnospiraceae</i> NK4A136group | rs59805249 | 0.1761682 | 0.08803291 | 0.0453748 |
| <i>Lachnospiraceae</i> NK4A136group | rs68104925 | 0.1748273 | 0.08766868 | 0.0461322 |
| <i>Lachnospiraceae</i> NK4A136group | rs7073658 | 0.171341 | 0.08759399 | 0.05045553 |
| <i>Lachnospiraceae</i> NK4A136group | rs73044693 | 0.1776147 | 0.08791729 | 0.04335768 |
| <i>Lachnospiraceae</i> NK4A136group | rs7616165 | 0.2066792 | 0.08961577 | 0.02109487 |
| <i>Lachnospiraceae</i> NK4A136group | rs76193507 | 0.1078952 | 0.10289159 | 0.29434833 |
| <i>Lachnospiraceae</i> NK4A136group | rs7832116 | 0.1580043 | 0.08744354 | 0.07077326 |
| <i>Lachnospiraceae</i> NK4A136group | rs954878 | 0.1683296 | 0.08762288 | 0.054723 |

Table S6 Metabolites of gut microbiota on PTB

| Gut Microbiota | Metabolite |
|---|------------------------|
| <i>Lachnospiraceae NK4A136</i> group | Indoxyl sulfate |
| | p-Cresol sulfate |
| | Phenylacetylglutamine |
| | 3-Indolepropionic acid |
| | Trimethylamine oxide |
| <i>Escherichia_Shigella</i> | Trimethylamine oxide |
| | Indoxyl sulfate |
| <i>Coproccoccus2</i> | 3-Indolepropionic acid |